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Gas chromatographic separation of enantiomeric amino acids and amines with α-methoxy-α-trifluoromethylpropionic acid as a chiral derivatizing agent

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Abstract

Enantiopure α-methoxy-α-trifluoromethylpropionic acid was prepared from 1,1,1-trifluoroacetone for the chiral separation of amino acids and amines by gas chromatography. Separation of the diastereomeric amide analytes was carried out on a capillary column coated with polyethylene glycol and showed good selectivity for these amino compounds at low column temperatures. A regularity was observed in the elution order, namely that a heterochiral diastereomer, *i.e.*, the *S,R*-isomer, eluted faster than the homochiral *S,S* counterpart.

1. Introduction

Although the direct separation of enantiomers by gas chromatography (GC) and high-performance liquid chromatography (HPLC) on chiral stationary phases has progressed greatly in the last decade [1–3], indirect separation *via* conversion into a pair of diastereomers by use of a chiral derivatizing agent (CDA) still remains a widely used and reliable method for the determination of enantiomeric purity and the assignment of absolute configuration by NMR and HPLC and less frequently by GC [4–7].

Among the variety of proposed CDAs [8–12], α-methoxy-α-trifluoromethylphenylacetic acid (MTPA) has been the most widely used for the derivatization of secondary alcohols and amines to the diastereomeric esters and amides [13,14]. However, CDAs that afford readily volatile diastereomers, amides in particular, suitable for GC analysis are limited, in spite of the fact that GC on an achiral column is operationally more advantageous than LC or NMR for the rapid analysis of many samples [15]. Ishikawa and co-workers developed two CDAs, perfluoro-2-propoxypropionic acid (PPPA) [16,17] and perfluoro-2-isopropoxypropionic acid (PIPA) [15], for the GC separation of 1-arylalkylamines and α-amino acids. Herein, we report that α-methoxy-α-trifluoromethylpropionic acid (MTPr), which can readily be prepared in an enantiopure form in substantial amounts, is an improved addition to these reagents for the separation of optically active amino acids and

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amines by achiral capillary GC at low operating temperatures [18].

2. Experimental

2.1. Apparatus

Gas chromatography was peformed using a Shimadzu GC-7AG instrument on the following fused-silica capillary columns: (A) CBJ17-W30-100 (30 m × 0.53 mm I.D. column coated with OV-17-type phenylmethylsilicone; Shimadzu); (B) Stabilwax (30 m × 0.25 mm I.D. column coated with Crossbonded Carbowax PEG; Restek) and (C) CBP20-W25-100 (25 m × 0.53 mm I.D. column coated with PEG-20M-type polyethylene glycol; Shimadzu). The instrument was equipped with a flame ionization detector and data collection was carried out on a Shimadzu C-R3A data processor. The splitting ratio was *ca.* 1:100 with the use of a Shimadzu-9 apparatus and the carrier gas was helium at 0.5 kg/cm^2. Liquid chromatography was performed using a Shimadzu LC-6A apparatus equipped with a Shimadzu SPD-6A ultraviolet detector (254 nm) on a 250 mm × 4.6 mm I.D. stainless-steel column packed with silica gel (Hitachi Gel 3056).

IR spectra were recorded on a Shimadzu IR-460 grating spectrophotometer. Optical rotations were measured on a Perkin-Elmer Model 241 polarimeter in a 10- or 1-cm thermostated microcell. ^{1}H NMR spectra were recorded on a Hitachi R-90H or JEOL JNM-FX 60 instrument with tetramethylsilane as internal standard. Melting points were measured on a Yamato MP-21 apparatus and are uncorrected.

2.2. Materials

1,1,1-Trifluoroacetone (Aldrich) was distilled before use. Enantiomeric amino acids, amines and alcohols used for derivatization were of commercial origin unless stated otherwise. (*S*)-2-Amino-4-phenylbutyric acid {$[\alpha]_D^{29}$ + 49.6° (*c* 1.27, 1 *M* HCl), 95% enantiomeric excess (ee)} [19] and (*S*)-2-amino-5-phenylvaleric acid {$[\alpha]_D^{26}$ + 19.4° (*c* 0.36, 1 *M* HCl)} [20] were prepared by the literature procedures. Amino acid methyl esters were prepared according to the conventional method by reaction with methanol–HCl or –thionyl chloride [21]. Tetrahydrofuran (THF) and benzene were distilled from sodium diphenylketyl. Carbon tetrachloride (CCl_4) and pyridine were distilled from CaH_2. Solvents used for HPLC were distilled before use. Column chromatography was performed using Nacalai Tesque silica gel 60.

2.3. Preparation of racemic MTPr (*3*)

1,1,1-Trifluoroacetone cyanohydrin

According to the method reported by Darrall *et al.* [22], 1,1,1-trifluoroacetone (**1**) (98.2 g, 877 mmol) was treated with sodium cyanide (44.3 g, 903 mmol). After the usual work-up, distillation gave 1,1,1-trifluoroacetone cyanohydrin (90.8 g, 75% yield) as a clear liquid, b.p. 53–58°C/27 mmHg (1 mm Hg = 133.322 Pa); IR (liquid film), 3400, 1920, 1620 cm^{-1}; ^{1}H NMR ($CDCl_3$), δ (ppm) 1.77 (3H, s, CH_3), 4.24 (1H, br, OH). The IR spectrum was devoid of the cyano group absorption, presumably owing to the strong electron-withdrawing effect of the CF_3 moiety.

α-Hydroxy-α-trifluoromethylpropionic acid (2)

The cyanohydrin (85.0 g, 612 mmol) was cautiously dissolved in concentrated H_2SO_4 (60 ml) at 70–80°C and the mixture was gradually heated to *ca.* 120°C, after which water was added (550 ml). After the mixture had been heated at reflux for 9 h, it was extracted with diethyl ether (× 5) and dried over $MgSO_4$. Removal of the solvent by distillation and crystallization from $CHCl_3$ gave α-hydroxy-α-trifluoromethylpropionic acid (**2**) as colourless crystals (66.8 g, 69.8% yield); m.p. 87–88°C (lit. [22] m.p., 88°C); IR (KBr), 3405, 3025, 1745, 1289, 1253, 1183, 1111 cm^{-1}; ^{1}H NMR (acetone-d_6), δ (ppm) 1.60 (3H, s, CH_3), 5.85 (2H, s, br, OH and COOH). The methyl signal was slightly split by a long-range coupling with the CF_3 group.

α-Methoxy-α-trifluoromethylpropionic acid (MTPr, 3)

Under nitrogen, to a stirred suspension of sodium hydride (38.2 g, 1.60 mol) in THF (240 ml) were added methyl iodide (74.4 ml, 1.22

mol) and then a solution of hydroxy acid **2** (60.0 g, 382 mmol) in THF (240 ml). After the mixture had been stirred overnight at room temperature, the bulk of the volatiles was removed by distillation. The residue was dissolved in water and washed with diethyl ether. The aqueous alkaline solution was made acidic by addition of concentrated HCl and extracted with portions of diethyl ether. The combined ether extracts were dried over $MgSO_4$ and distillation gave **3** as a clear liquid (55.7 g, 84.8% yield), b.p. 100.5°C/25 mmHg; IR (liquid film), 3208, 3016, 2984, 1742, 1188 cm^{-1}; ^1H NMR ($CDCl_3$), δ (ppm) 1.68 (3H, s, CH_3), 3.50 (3H, s, OCH_3), 5.74 (1H, s, COOH). The methyl and methoxy signals were slightly split by long-range coupling with the CF_3 group.

2.4. Optical resolution of racemic MTPr (3) via (S)-1-phenylethylamides

Preparation of the diastereomeric amides by reaction with (S)-1-phenylethylamine

Racemic acid **3** (55.7 g, 318 mmol) was boiled with thionyl chloride (50 ml) for 24 h. Distillation of the reaction mixture under atmospheric pressure afforded the acid chloride of **3** (38.1 g, 62% yield) as a pale-yellow liquid, b.p. 115–117°C; IR (liquid film), 2960, 1796, 1462, 1302, 1188, 1112, 958, 790, 690 cm^{-1}; ^1H NMR ($CDCl_3$), δ (ppm) 1.67 (3H, s, CH_3), 3.52 (3H, s, OCH_3).

The acid chloride was used for reaction with (*S*)-1-phenylethylamine (29.0 g, 240 mmol) in CCl_4 (250 ml) and pyridine (40 ml) in the presence of 4-dimethylaminopyridine (DMAP) (1.27 g, 10.4 mmol). After the reaction mixture had been stirred for several hours at room temperature, it was diluted with diethyl ether and washed successively with portions of 2 *M* HCl, saturated $NaHCO_3$ and saturated brine and then dried over $MgSO_4$. Removal of the solvent gave 1-phenylethylamides **4** as a colourless solid (46.8 g, 85%).

Separation of amides into components

The mixture of the diastereomeric amides was recrytallized twice from hexane to afford the *R*, *S*-diastereomer as needles of essentially 100% diastereomeric excess (de), as evidenced by GC on column C, 11.9 g (51% yield based on the enantiomeric **3**); m.p. 99.4–100°C; $[\alpha]_D^{20}$ −88.9° ($CHCl_3$, *c* 0.97); IR (KBr), 3315, 1661, 1528 cm^{-1}; ^1H NMR ($CDCl_3$), δ (ppm) 1.51 (3H, d, $J = 6.82$ Hz, CH_3), 1.59 (3H, s, CH_3), 3.38 (3H, s, OCH_3), 5.61 (1H, m, C–H), 7.02 (1H, br, N–H), 7.32 (5H, s, C_6H_5). The absolute stereochemistry of the amide as *R*, *S* was determined by X-ray crystallographic analysis, the details of which will be reported elsewhere [23].

The mother liquors from the above crystallizations were combined and the solvents were distilled off. The residue (34.5 g) was chromatographed on a silica gel column (1 kg) with ethyl acetate–hexane (3:10) as the eluent to give the following fractions after distillation of the solvent: (1) 6.10 g (*R*, *S*-isomer of 99.4% de); (2) 5.09 g (*R*, *S*, 90.6% de); (3) 2.85 g (*S*,*S*, 97.0% de); (4) 18.43 g (*S*,*S*, 100% de). The last diastereomerically pure (*S*,*S*)-**4** fraction had the following physical data: m.p. 40.4–41°C; $[\alpha]_D^{20}$ −43.8° ($CHCl_3$, *c* 1.04); IR (KBr), 3310, 3315, 1663, 1533, 1309, 1180, 1144, 1100, 1043, 767, 698 cm^{-1}; ^1H NMR ($CDCl_3$), δ (ppm) 1.52 (3H, d, $J = 6.82$ Hz, CH_3), 1.64 (3H, s, CH_3), 3.45 (3H, s, OCH_3), 5.11 (1H, m, C–H), 7.22 (1H, br, N–H), 7.30 (5H, s, C_6H_5).

Hydrolysis of (S,S)-4 to enantiopure (S)-(+)-MTPr

Diastereopure (*S*,*S*)-**4** (18.4 g, 66.8 mmol) was dissolved in concentrated H_2SO_4 (185 ml) and stirred for 3 h at room temperature. This was slowly poured into ice–water (1.1 l) and extracted with portions of diethyl ether. After drying over $MgSO_4$, the solvent was distilled off to leave a solid (13.0 g), which was boiled in a solution of KOH (37.5 g) in methanol (150 ml) and water (12.5 ml) for 7 h. The mixture was diluted with water and washed with several portions of diethyl ether. The aqueous layer was made acidic by addition of concentrated H_2SO_4 and extracted with diethyl ether. After drying over $MgSO_4$, the solvent was distilled off. Distillation of the residue under reduced pressure afforded (*S*)-(+)-**3** as a colourless liquid (8.58 g,

75% yield), b.p. 93.1°C/18 mmHg; d_4^{18} 1.32; $[\alpha]_D^{20}$ + 4.29°, $[\alpha]_{365}^{20}$ + 13.9° (neat); $[\alpha]_D^{20}$ + 4.88° (CH_3OH, *c* 3.63); IR (liquid film), 3216, 3012, 2980, 1736, 1464, 1312, 1166, 1045, 684 cm^{-1}; ^1H NMR ($CDCl_3$), δ (ppm) 1.67 (3H, s, CH_3), 3.53 (3H, s, OCH_3), 7.49 (1H, br, COOH).

The acid chloride of (*S*)-**3** [(*S*)-MTPr-Cl] was prepared as above by treatment with thionyl chloride and distillation, and divided into small glass ampoules for storage. A sample of (*S*)-MTPr-Cl was treated with 3,5-dinitroaniline in THF and triethylamine in the presence of DMAP to give the 3,5-dinitroanilide according to the method described previously [24]. HPLC of the anilide on a chiral stationary phase prepared in this laboratory by bonding (*S*)-1,1'-binaphthyl-2,2'-dicarboxylic acid to 3-aminopropylsilanized silica showed that the enantiomeric purity of the sample should be more than 99.5% ee [24]. The relevant chromatographic data for the anilide from partially active **3** were as follows: eluent, 2-propanol–hexane (15:85); flow-rate, 1 ml/min; capacity factor (*k'*) of (*R*)-**3** anilide = 4.32; *k'* of *S*-isomer = 3.78.

Hydrolysis of (R,S)-4 to enantiopure (R)-(−)-MTPr

Diastereomer (*R,S*)-**4** (2.65 g, 9.63 mmol) was treated as above to give (*R*)-**3** (1.06 g, 64%) after distillation, b.p. 95°C/24 mmHg; $[\alpha]_D^{20}$ −4.31°, $[\alpha]_{578}^{20}$ −4.48°, $[\alpha]_{546}^{20}$ −5.11°, $[\alpha]_{436}^{20}$ −8.69°, $[\alpha]_{365}^{20}$ −14.0° (neat).

2.5. Preparation of diastereomeric MTPr amide analytes

In a vial blown with dry nitrogen were placed a partially active amine (or an amino acid methyl ester) adjusted to 20–25% ee (30–50 mg), THF (1.5 ml), triethylamine (0.5 ml), DAMP (10 mg) and then (*S*)-MTPr-Cl (1.5 equiv.). After the mixture had been stirred overnight at room temperature, it was diluted with diethyl ether and successively washed with 2 *M* HCl, 5% aqueous NH_3 and brine and dried over $MgSO_4$. The solvents were removed under reduced pressure to give a sample of the MTPr amide analyte. When only one enantiomeric amino compound was available, derivatization was carried out by using partially active (*S*)-MTPr-Cl (*ca.* 25% ee). These data were also presented as if derivatization had been carried out by using partially active amino compounds and enantiopure (*S*)-MTPr-Cl for the sake of clarity [25].

Test of kinetic resolution during derivatization

DL-Glutamic acid dimethyl ester was derivatized as above; the flame ionization detection (FID) response of the diastereomers on column C was 50.39:49.61 (see Fig. 2). The analyte prepared from (*R*)-1-phenylethylamine of 25.0% ee showed two peaks with FID intensities of 62.78:37.22, respectively (see Table 3).

3. Results and discussion

3.1. Preparation of enantiopure (S)-(+)-MTPr

Treatment of 1,1,1-trifluoroacetone (**1**) with sodium cyanide according to the method of Darrall *et al.* [22] readily afforded the corresponding cyanohydrin, acid hydrolysis of which gave α-hydroxy-α-trifluoromethylpropionic acid (**2**) as colourless crystals (Fig. 1). Darrall *et al.* [22] resolved **2** into the enantiomers by fractional crystallization of the brucine salt, but attempts to resolve **2** by use of several chiral amines including brucine turned out to be very ineffective and another route to optically pure MTPr was desired for practical synthesis.

Selective methylation of the hydroxyl function of acid **2** by treatment with methyl iodide and sodium hydride in THF afforded (±)-MTPr (**3**) in good yield. Optical resolution of **3** could be accomplished according to essentially the same method as used for the resolution of PPPA [17]. After conversion of **3** into the diastereomeric amides **4** with (*S*)-1-phenylethylamine, they were separated into the diastereomers (*R,S*)-**4** and (*S,S*)-**4** by crystallization from hexane and silica gel column chromatography. The absolute stereochemistry of the acid part of the (*R,S*)-amide was determined by reference to the *S* configuration of the 1-phenylethylamine based

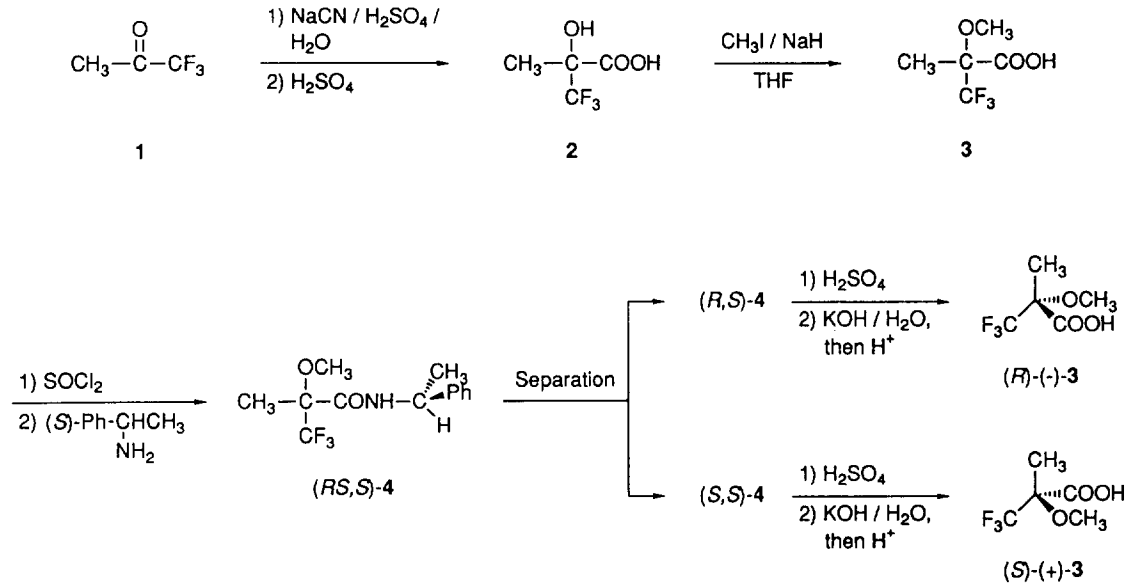

Fig. 1. Scheme of synthesis.

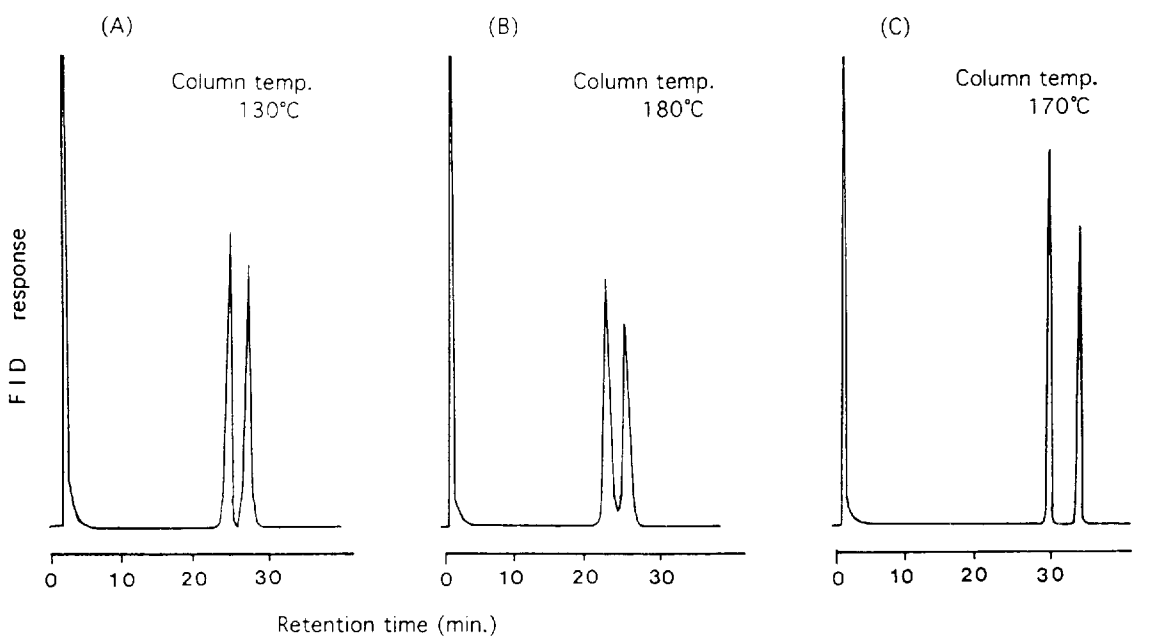

Fig. 2. GC separation of MTPr amides derived from racemic dimethyl glutamate on fused-silica capillary columns coated with (A) phenylmethylsilicone (CBJ17-W30-100), (B) Carbowax (Stabilwax) and (C) polyethylene glycol (CBP20-W25-100) (see Experimental for details). Carrier gas. He at 0.5 kg/cm^2.

on X-ray crystallographic structure analysis, and the relevant experimental details will be reported elsewhere [23].

Treatment of (*S*,*S*)-**4** with concentrated sulfuric acid followed by alkaline hydrolysis and distillation afforded enantiopure (*S*)-(+)-MTPr as a clear liquid for the first time. Boiling (*S*)-MTPr with thionyl chloride followed by distillation gave the acid chloride [(*S*)-MTPr-Cl] as a pale-yellow liquid, which was divided into small glass ampoules for storage. Enantiomeric homogeneity of the acid chloride (>99.5% ee) was confirmed by HPLC analysis on an axially chiral binaphthalene-based stationary phase after conversion into the 3,5-dinitroanilide [24]. Similar treatment of (*R*,*S*)-**4** gave enantiopure (*R*)-(−)-MTPr.

Although the optical resolution of MTPr required the formation of the diastereomeric 1-phenylethylamides and removal of the amine auxiliary, this in turn permitted a ready improvement in the optical purity of the MTPr as desired. It should be recalled that commercially available, but expensive, MTPA is an oil of 97.9–99.7% ee, which imposes an inevitable chiral discrimination limit [26].

3.2. GC separation of enantiomeric amino acids and amines as the MTPr amides

At first, the inherent possibility of fractionation accompanying chiral derivatization was checked with the use of MTPr. A sample of racemic dimethyl glutamate was *N*-acylated with an excess of (*S*)-MTPr-Cl in THF and triethylamine in the presence of DMAP by stirring overnight at room temperature in a capped vial. The derivatized glutamide sample was obtained after the usual work-up and subjected to GC analysis. Fig. 2 shows the chromatograms for the separation of the glutamide diastereomers on three different capillary columns coated with a silicone oil (column A), carbowax (column B) and polyethylene glycol (column C). Although

Table 1
GC separation of diastereomeric MTPr amides derived from enantiomeric amino acid methyl esters

Run No.	Amino acid	Column temperature (°C)	k'		α	R_s
			(*S*,*S*)	(*R*,*S*)		
1	Alanine	140	9.67	7.56	1.27	4.70
2	Valine	140	10.59	8.63	1.23	5.00
3	Leucine	140	16.13	12.58	1.28	6.84
4	Isoleucine	140	15.06	12.21	1.23	4.29
5	Norleucine	140	20.94	16.85	1.24	8.43
6	Aspartic acid[a]	170	20.66	18.21	1.13	2.94
7	Glutamic acid[a]	170	37.86	32.97	1.15	4.28
8	Phenylglycine	170	13.51	9.87	1.37	–[b]
9	Phenylalanine	200	13.85	12.58	1.10	2.76
10	EtCHCOOH | NH_2	140	11.09	8.85	1.25	5.48
11	$Ph(CH_2)_2CHCOOH$ | NH_2	200	25.16	21.90	1.15	5.00
12	$Ph(CH_2)_3CHCOOH$ | NH_2	200	32.46	29.05	1.12	4.00

Column, CBP20-W25-100; carrier gas, helium at 0.5 kg/cm^2; k' = capacity factor; α = separation factor, R_s = resolution.
[a] Dimethyl ester.
[b] Epimerization occurred, see text.

all of these columns separated the diastereomers, column C seemed the best considering the column performance, which included separability and column temperature required. The difference in the FID response between the diastereomeric pair of the glutamides was 0.78% on this column, which may be regarded as within the experimental error of integration. Another separation of the diastereomeric MTPr amides prepared from 1-phenylethylamine of 25.0% ee showed the difference in FID response to be less than 0.60%. These results suggest that the standard precautions will substantially reduce the kinetic resolution problem.

Twelve partially active amino acid methyl esters were acylated with (*S*)-MTPr-Cl as above and the results of the GC separation of these analytes are summarized in Table 1. Complete baseline separation was attained with all amide pairs tested except derivatized phenylglycine (run 8) (see below). It is noted that a resolution (R_s) larger than 8 was attained for norleucine (run 5). As an α value (separation factor) of 1.02 or greater is considered to be of practical application in chiral discrimination by capillary GC, hence it can be said that MTPr is an excellent CDA for discrimination of these amino acids. To demonstrate the selectivity obtainable with MTPr, a simultaneous separation of a mixture composed of seven diastereomeric pairs of MTPr amides prepared from the corresponding α-amino acid methyl esters is shown in Fig. 3. Under the conditions employed, all the diastereomeric pairs could be separated in a single temperature-programmed run within a short period, although partial overlap of the peaks of L-leucine and D-norleucine occurred.

The data in Table 1 reveal that in all instances heterochiral diastereomers, i.e., *R,S* pairs, elute faster than the *S,S* counterparts. At present we cannot deduce any mechanisms concerning the regularity of the elution orders, while it may still be of use in assigning the absolute configurations of amino acids. Fig. 4 compares the chiral discrimination ability of MTPr with that of the perfluoro analogue, PPPA. It is seen that the MTPr amides derived from phenylalanine methyl ester separate well but the PPPA amides not at

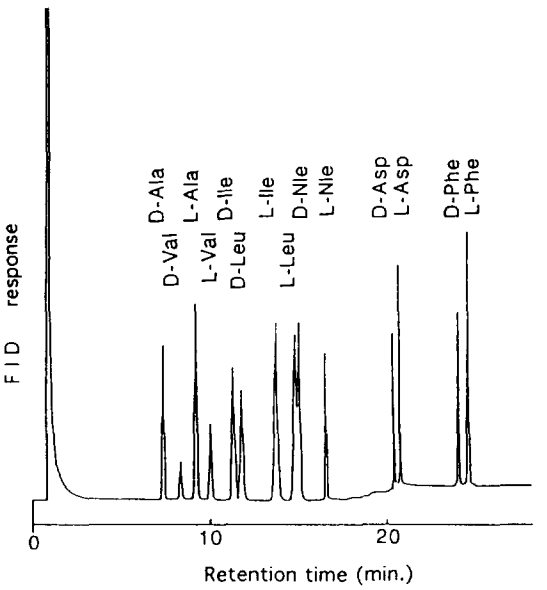

Fig. 3. GC separation of a mixture composed of seven diastereomeric pairs of MTPr amides prepared from the corresponding α-amino acid methyl esters. Conditions: column, CBP20-W25-100; carrier gas, He at 0.5 kg/cm^2; column temperature, programmed from 140 to 220°C, 16°C/min starting 14 min after the injection.

all on column C, although the latter elutes at a lower column temperature than the former.

Fig. 5A shows the elution behaviour of the MTPr amides derived from partially active phenylglycine methyl ester. The chromatogram shows a plateau with a small peak between the

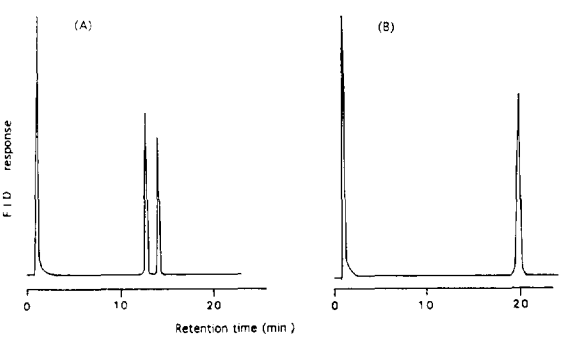

Fig. 4. Comparison of the separation of MTPr amides and PPPA amides derived from enantiomeric phenylalanine methyl ester. Conditions: column, CBP20-W25-100; carrier gas, He at 0.5 kg/cm^2; column temperature, (A) 200 and (B) 120°C.

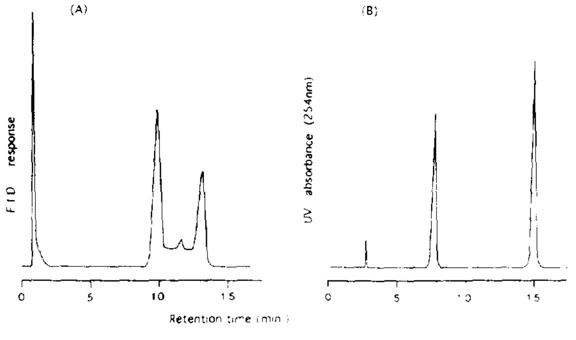

Fig. 5. GC and HPLC separation of MTPr amides derived from phenyglycine methyl ester. (A) GC separation on column CBP20-W25-100; carrier gas, He at 0.5 kg/cm^2; column temperature, 170°C. (B) HPLC separation on silica gel column; eluent, 2-propanol–hexane (1:99) at 1 ml/min; detection, UV at 254 nm.

two diastereomeric peaks, indicating the occurrence of epimerization of the diastereomers during the elution [27]. This may be ascribed to the presence of a labile hydrogen on the chiral carbon atom of the amino acid residue activated by the co-existing phenyl substituent. In such a case, however, HPLC separation is an alternative resort, as Fig. 5B and Table 2 indicate, by using a phenyl nucleus as the UV-responsive moiety. Good selectivity as shown by the α and R_s values is noticeable and, interestingly, *S,S*-diastereomers eluted faster than the *R,S* counterparts, indicating that the mechanism of chiral discrimination of these MTPr amides by normal-phase HPLC is different from that by capillary column GC.

Table 3 summarizes the results of the GC separation of eleven partially active amines and four alcohols. For all the amines examined, chiral separation was attained, better selectivity being obtained with alkylarylamines than with simple alkylamines. It should be noted that there seems to be no report on the application of the Ishikawa and co-workers' PPPA and PIPA to GC separation of such simple alkylamines. As can be seen in Table 3, the separability of the diastereomeric esters is inferior to that of the amides. Hence, MTPr may be used more advantageously for the GC separation of amino compounds than that of alcohols [7]. With respect to the elution order of these amides and esters, here again the *R,S*-diastereomers always eluted before the *S,S* counterparts.

4. Conclusions

A practical method has been developed for the preparation of enantiopure MTPr, which in turn has been demonstrated to be an efficient CDA

Table 2
HPLC separation of diastereomeric MTPr amides derived from amino acids methyl esters bearing a phenyl group

Run No.	Amino acid	k'		α	R_s
		(*S*, *S*)	(*R*, *S*)		
1	Phenylglycine	1.38	3.52	2.55	7.23
2	Phenylalanine	2.27	3.86	1.70	5.67
3	$Ph(CH_2)_2CH(NH_2)COOH$	2.34	4.11	1.76	10.00
4	$Ph(CH_2)_3CH(NH_2)COOH$	1.87	3.55	1.90	11.27

Conditions: mobile phase, 2-propanol–hexane (1:99); flow-rate 1 ml/min; column, silica gel (250 mm × 4.6 mm I.D.); detection, UV at 254 nm.

Table 3
GC separation of diastereomeric MTPr amides derived from enantiomeric amines and alcohols

Run No.	Amine or alcohol	Column temperature (°C)	k'		α	R_s
			(*S*,*S*)	(*R*,*S*)		
1	$PhCH(NH_2)CH_3$	160	14.67	12.45	1.18	5.71
2	$(1\text{-Naph})CH(NH_2)CH_3$	210	23.84	19.42	1.23	6.19
3	$(2\text{-Naph})CH(NH_2)CH_3$	210	25.15	24.14	1.04	4.92
4	$C_2H_5CH(NH_2)CH_3$	100	8.38	7.99	1.05	0.70
5	$c\text{-Hexyl}CH(NH_2)CH_3$	110	38.60	36.77	1.05	1.89
6	$n\text{-}C_5H_{11}CH(NH_2)CH_3$	120	12.26	11.27	1.09	0.89
7	3-(Aminomethyl)pinane	150	41.46	39.26	1.05	1.17
8	Menthylamine	160	7.84	7.04	1.11	2.00
9	Bornylamine	160	8.87	7.98	1.11	2.94
10	Isobornylamine	160	10.16	9.31	1.09	2.00
11	$Ph(CH_2)_2CH(NH_2)CH_3$	220	15.74	14.94	1.05	1.35
12	$n\text{-}C_6H_{13}CH(OH)CH_3$	80	26.33	25.36	1.04	0.57
13	Menthol	100	25.15	24.24	1.04	0.90
14	Borneol	100	28.56	28.56	1.00	0
15	$PhCH(OH)CH_3$	110	30.96	29.41	1.05	1.30

See Table 1 for GC conditions.

for the GC discrimination of enantiomeric amino acids and amines. It should be noted that MTPr is a low-boiling variant of MTPA in which a methyl substituent replaces the phenyl residue, and hence it is a potential CDA for the chiral discrimination of enantiomeric amino compounds by not only GC but also by ^{1}H and ^{19}F NMR [23]. It should also be noted that MTPr does not bear an α-hydrogen or α-fluorine on the carbon atom adjacent to the carboxylic function, which may cause racemization during the derivatization or high toxicity [4].

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